## I. AMENDMENTS TO THE SPECIFICATION

Please replace paragraphs as filed with the following replacement paragraphs:

**[00154]** Examples of cleavable oligonucleotides which contain two reverse U (rU) linkers and have been synthesized on a chip are as follows:

| Probe | Pu1 PS1 PU2 PS2 |
|---|---|
| IL6_T7 | 5'CAAGGATCTTACCGCTGTTGtgaggagacttgcctggtgrUTAATACGACTCACTATAGGt ctgcaggaactggatcaggrU (SEQ ID NO:1) |
| CYP11A_t7 | 5'CAAGGATCTTACCGCTGTTGgtgaccctgcagagatatctrUTAATACGACTCACTATAGGgttccggaag taggtgatgtrU(SEQ ID NO:2) |
| ATP2A1_T7 | 5'CAAGGATCTTACCGCTGTTGgattggcattgccatgggatrUTAATACGACTCACTATAGGtccacagcagctacgatggrU (SEQ ID NO:3) |
| IL6_Nick | 5'caaggatctt accgctgttg tgaggagact tgcctggtgn cgctccagac ttgagtccga tctgcaggaa ctggatcaggrU (SEQ ID NO:4) |
| CYP11A_Nick | 5'CAAGGATCTTACCGCTGTTGgtgaccctgcagagatatctrUCGCTCCAGACTTGAGTCCGAgttccggaa gtaggtgatgtrU (SEQ ID NO:5) |
| ATP2A1_Nick | 5'CAAGGATCTTACCGCTGTTGgattggcattgccatgggatrUCGCTCCAGACTTGAGTCCGAtccacagcagctacgatggrU (SEQ ID NO:6) |

**[00164]** Different strategies can be used to release or cleave oligonucleotides synthesized on a solid substrate from that substrate. The cleavage efficiency of three different linkers was examined to determine the preferred linker(s) for cleaving oligonucleotides from a solid substrate (rU is 5'-phosphoramidite with 2'-acetyl and 3'DMT; U is 3'-phosphoramidite with 2'fpmp and 5'-DMT; and dU is 2'-deoxyuridine). To begin, the following oligonucleotides were synthesized using an Expetide™ DNA synthesizer and standard phosphoamidite chemistry:

Sequence A 3'ttttttttttrugtccacagcatccga-fam-5' (SEQ ID. NO:7)

Sequence B 3'ttttttttttugtccacagcatccga-fam-5' (SEQ ID. NO:8)

Sequence C 3' ttttttttttdugtccacagcatccga-fam-5' (SEQ ID. NO:9)

**[00168]** The GFP gene is 714 base pairs (bp) long. Suitable subchains (computational fragmentation) for the assembly of the GFP gene were selected, and oligonucleotides between 40 and 47 nucleotides long were synthesized on a chip using the methods outlined above. The complete set of 34 GFP subchains synthesized on a chip are as follows:

| | | |
|---|---|---|
| GFP-F2 | ATGAGTAAAG GAGAAGAACT TTTCACTGGA GTTGTCCCAA TTCTTG | SEQ ID NO:10 |
| GFP-F3 | TTGAATTAGA TGGTGATGTT AATGGGCACA AATTTTCTGT CAGT | SEQ ID NO:11 |
| GFP-F4 | GGAGAGGGTG AAGGTGATGC AACATACGGA AAACTTACCC T | SEQ ID NO:12 |
| GFP-F5 | TAAATTTATT TGCACTACTG GAAAACTACC TGTTCCATGG CCAA | SEQ ID NO:13 |
| GFP-F6 | CACTTGTCAC TACTTTCTCT TATGGTGTTC AATGCTTTTC AAGATA | SEQ ID NO:14 |
| GFP-F7 | CCCAGATCAT ATGAAACGGC ATGACTTTTT CAAGAGTGCC AT | SEQ ID NO:15 |
| GFP-F8 | GCCCGAAGGT TATGTACAGG AAAGAACTAT ATTTTTCAAA GATG | SEQ ID NO:16 |
| GFP-F9 | ACGGGAACTA CAAGACACGT GCTGAAGTCA AGTTTGAAGG T | SEQ ID NO:17 |
| GFP-F10 | GATACCCTTG TTAATAGAAT CGAGTTAAAA GGTATTGATT TTAAAG | SEQ ID NO:18 |
| GFP-F11 | AAGATGGAAA CATTCTTGGA CACAAATTGG AATACAACTA TAACTC | SEQ ID NO:19 |
| GFP-F12 | ACACAATGTA TACATCATGG CAGACAAACA AAAGAATGGA ATCAA | SEQ ID NO:20 |
| GFP-F13 | AGTTAACTTC AAAATTAGAC ACAACATTGA AGATGGAAGC GTTCA | SEQ ID NO:21 |
| GFP-F14 | ACTAGCAGAC CATTATCAAC AAAATACTCC AATTGGCGAT GG | SEQ ID NO:22 |
| GFP-F15 | CCCTGTCCTT TTACCAGACA ACCATTACCT GTCCACACAA T | SEQ ID NO:23 |
| GFP-F16 | CTGCCCTTTC GAAAGATCCC AACGAAAAGA GAGACCACAT G | SEQ ID NO:24 |
| GFP-F17 | GTCCTTCTTG AGTTTGTAAC AGCTGCTGGG ATTACACATG GC | SEQ ID NO:25 |
| GFP-F18 | ATGGATGAAC TATACAAATA GCATTCGTAG AATTGACTCT ATAGTG | SEQ ID NO:26 |
| GFP-R1 | TGAAAAGTTC TTCTCCTTTA CTCAT | SEQ ID NO:27 |
| GFP-R2 | ATTAACATCA CCATCTAATT CAACAAGAAT TGGGACAACT CCAG | SEQ ID NO:28 |
| GFP-R3 | CATCACCTTC ACCCTCTCCA CTGACAGAAA ATTTGTGCCC | SEQ ID NO:29 |
| GFP-R4 | TTTCCAGTAG TGCAAATAAA TTTAAGGGTA AGTTTTCCGT ATGTTG | SEQ ID NO:30 |
| GFP-R5 | ATAAGAGAAA GTAGTGACAA GTGTTGGCCA TGGAACAGGT AGT | SEQ ID NO:31 |
| GFP-R6 | GCCGTTTCAT ATGATCTGGG TATCTTGAAA AGCATTGAAC ACC | SEQ ID NO:32 |
| GFP-R7 | CCTGTACATA ACCTTCGGGC ATGGCACTCT TGAAAAAGTC AT | SEQ ID NO:33 |
| GFP-R8 | ACGTGTCTTG TAGTTCCCGT CATCTTTGAA AAATATAGTT CTTT | SEQ ID NO:34 |
| GFP-R9 | CGATTCTATT AACAAGGGTA TCACCTTCAA ACTTGACTTC AGC | SEQ ID NO:35 |
| GFP-R10 | TGTCCAAGAA TGTTTCCATC TTCTTTAAAA TCAATACCTT TTAACT | SEQ ID NO:36 |
| GFP-R11 | TGCCATGATG TATACATTGT GTGAGTTATA GTTGTATTCC AATTTG | SEQ ID NO:37 |
| GFP-R12 | TTGTGTCTAA TTTTGAAGTT AACTTTGATT CCATTCTTTT GTTTGTC | SEQ ID NO:38 |
| GFP-R13 | TTGTTGATAA TGGTCTGCTA GTTGAACGCT TCCATCTTCA ATG | SEQ ID NO:39 |
| GFP-R14 | TGTCTGGTAA AAGGACAGGG CCATCGCCAA TTGGAGTATT | SEQ ID NO:40 |
| GFP-R15 | GGGATCTTTC GAAAGGGCAG ATTGTGTGGA CAGGTAATGG T | SEQ ID NO:41 |
| GFP-R16 | CTGTTACAAA CTCAAGAAGG ACCATGTGGT CTCTCTTTTC GTT | SEQ ID NO:42 |
| GFP-R17 | TGCTATTTGT ATAGTTCATC CATGCCATGT GTAATCCCAG CAG | SEQ ID NO:43 |

**[00169]** Additionally, the following two control oligonucleotides (Puc2PM- perfect match and Puc2MM- mismatch) were also synthesized on the chip using the methods outlined above:

| | | |
|---|---|---|
| PUC2PM | CTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTA | SEQ ID NO:44 |
| PUC2MM | CTGGCAGTAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTA | SEQ ID NO:45 |

**[00179]** One method for releasing or cleaving synthesized oligonucleotides from a solid substrate is an enzymatic approach involving the use of restriction endonuclease (R.E.) enzymes to selectively and specifically cleave desired oligonucleotides from the substrate surface. To test this approach, the Dpn II R.E. enzyme was used to cleave two complementary oligonucleotide DNAs, the first oligo being GFP-F2Part 5'-CACTGGAGTTGTCCCAATTCTTGgatcggcc-3' (SEQ ID NO:46) and the second one being DpnIISite 5'-ggccgatcCAA-3' (SEQ ID NO:47). Since II enzyme recognizes and cleaves the sequence 5'-^GATC-3', the isolation of clean oligonucleotides was expected after digestion with the enzyme. Our initial test on the digested oligonucleotides in solution phase was successful. In the experiment, two oligonucleotides were mixed at a molar ration of 1:5 (GFP-F2Part:DpnIISite) and incubated with or without Dpn II enzyme at 37°C. These reactions were analyzed at various time points with CE (capillary electrophoresis, 10% polyacryliamid gel with 7 M urea). As shown in Figure 23, approximately 80% of the longer oligonucleotides were cut by Dpn II in 1 hour. This experiment demonstrates the efficient release of synthesized oligonucleotides from the substrate surface through the use of R.E. enzymes.

**[00180]** In other embodiments of the present disclosure, an oligonucleotide sequence can be synthesized such that it will anneal itself, thereby forming a duplex oligonucleotide with a hairpin loop. The duplex DNA can then be digested with an enzyme, for example a R.E. enzyme, to form double-stranded DNA that can be ligated to other double-stranded DNA and/or oligonucleotides. To demonstrate the ability of a R.E. enzyme to digest a synthesized oligonucleotide that anneals to itself, the following oligonucleotide sequences with FAM label (DEFINE FAM) were synthesized on a chip with a regular DMT chip surface:

| | | |
|---|---|---|
| ePM-40 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTAAATGCCGCATAGTTAAAGTGGCTGCTGCCAG | SEQ ID NO:48 |
| ePM-20 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTAAATGCCGCATA | SEQ ID NO:49 |

| | | |
|---|---|---|
| eMM-40 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTACATGCCGCATAGTTAAAGTGGCTGCTGCCAG | SEQ ID NO:50 |
| eMM-40-2 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTACATGCCGCATAGTTAAAGTGGCCGCTGCCAG | SEQ ID NO:51 |
| eMM-20 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTACATGCCGCATA | SEQ ID NO:52 |
| eD-40 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTAATGCCGCATAGTTAAAGTGGCTGCTGCCAG | SEQ ID NO:53 |
| eD-40-2 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTAATGCCGCATAGTTAAAGTGGCGCTGCCAG | SEQ ID NO:54 |
| eD-20 | FAM-<br>CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGATCGGCCTTTTGGCCGATCGCAT<br>AGTTAATGCCGCATA | SEQ ID NO:55 |

**[00183]** This efficiency of the PGA chemistry utilized in the present disclosure also results in the ability of this chemistry to generate synthetic oligonucleotide sequences that are significantly longer than those that could be synthesized using previously disclosed methods. A programmable light-directed synthesis system was used to synthesize oligomers up to 100 nucleotides in length on a microfluidic array chip. The oligonucleotides synthesized on a chip were as follows:

| | | |
|---|---|---|
| PU2PM-100 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT<br>ATGCGGCATTAACTATGCGGCATTTAACTATGC | SEQ ID NO:56 |
| Pu2PM-95 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT<br>ATGCGGCATTAACTATGCGGCATTTAAC | SEQ ID NO:57 |
| Pu2PM-90 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT<br>ATGCGGCATTAACTATGCGGCAT | SEQ ID NO:58 |
| Pu2PM-85 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT<br>ATGCGGCATTAACTATGC | SEQ ID NO:59 |
| Pu2PM-80 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT<br>ATGCGGCATTAAC | SEQ ID NO:60 |
| Pu2PM-75 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT<br>ATGCGGCAT | SEQ ID NO:61 |
| Pu2PM-70 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT<br>ATGC | SEQ ID NO:62 |
| Pu2PM-65 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:63 |
| Pu2PM-60 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:64 |
| Pu2PM-55 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:65 |
| Pu2PM-50 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:66 |
| Pu2PM-45 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:67 |
| Pu2PM-40 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:68 |
| Pu2PM-35 | CTGGCAGCAGCCACTTTAACTATGCGGCATTTAAC | SEQ ID NO:69 |
| Pu2PM-30 | CTGGCAGCAGCCACTTTAACTATGCGGCAT | SEQ ID NO:70 |
| Pu2PM-25 | CTGGCAGCAGCCACTTTAACTATGC | SEQ ID NO:71 |
| Pu2PM-20 | CTGGCAGCAGCCACTTTAAC | SEQ ID NO:72 |

| | | |
|---|---|---|
| Pu2P M-15 | CTGGCAGCAGCCACT | SEQ ID NO:73 |
| Pu2M M-100 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT ATGCGGCATTAACTATGCGGCATTTAACTATGC | SEQ ID NO:74 |
| Pu2M M-95 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT ATGCGGCATTAACTATGCGGCATTTAAC | SEQ ID NO:75 |
| Pu2M M-90 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT ATGCGGCATTAACTATGCGGCAT | SEQ ID NO:76 |
| Pu2M M-85 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT ATGCGGCATTAACT ATGC | SEQ ID NO:77 |
| Pu2M M-80 | CTGGCAGTAGCCACTTTAACTATGCGGCAT TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTAAC | SEQ ID NO:78 |
| Pu2M M-75 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT ATGCGGCAT | SEQ ID NO:79 |
| Pu2M M-70 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACT ATGC | SEQ ID NO:80 |
| Pu2M M-65 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:81 |
| Pu2M M-60 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:82 |
| Pu2M M-55 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:83 |
| Pu2M M-50 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:84 |
| Pu2M M-45 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:85 |
| Pu2M M-40 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:86 |
| Pu2M M-35 | CTGGCAGTAGCCACTTTAACTATGCGGCATTTAAC | SEQ ID NO:87 |
| Pu2M M-30 | CTGGCAGTAGCCACTTTAACTATGCGGCAT | SEQ ID NO:88 |
| Pu2M M-25 | CTGGCAGTAGCCACTTTAACTATGC | SEQ ID NO:89 |
| Pu2M M-20 | CTGGCAGTAGCCACTTTAAC | SEQ ID NO:90 |
| Pu2M M-15 | CTGGCAGTAGCCACT | SEQ ID NO:91 |
| Puc2D -100 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTA TGCGGCATTAACTATGCGGCATTTAACTATGC | SEQ ID NO:92 |
| Puc2D -95 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTA TGCGGCATTAACTATGCGGCATTTAAC | SEQ ID NO:93 |
| Puc2D -90 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTA TGCGGCATTAACTATGCGGCAT | SEQ ID NO:94 |
| Puc2D -85 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTA TGCGGCATTAACTATGC | SEQ ID NO:95 |
| Puc2D -80 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTA TGCGGCATTAAC | SEQ ID NO:96 |
| Puc2D -75 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTA TGCGGCAT | SEQ ID NO:97 |
| Puc2D -70 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTA TGC | SEQ ID NO:98 |
| Puc2D -65 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:99 |
| Puc2D -60 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:100 |
| Puc2D -55 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:101 |
| Puc2D -50 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:102 |
| Puc2D -45 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:103 |
| Puc2D -40 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:104 |

| | | |
|---|---|---|
| Puc2D -35 | CTGGCAGAGCCACTTTAACTATGCGGCATTTAAC | SEQ ID NO:105 |
| Puc2D -30 | CTGGCAGAGCCACTTTAACTATGCGGCAT | SEQ ID NO:106 |
| Puc2D -25 | CTGGCAGAGCCACTTTAACTATGC | SEQ ID NO:107 |
| Puc2D -20 | CTGGCAGAGCCACTTTAAC | SEQ ID NO:108 |
| Puc2D -15 | CTGGCAGAGCCACT | SEQ ID NO:109 |
| Stem-85 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTAACTATGC | SEQ ID NO:110 |
| Stem-80 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTAAC | SEQ ID NO:111 |
| Stem-75 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:112 |
| Stem-70 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:113 |
| Stem-65 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:114 |
| Stem-60 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:115 |
| Stem-55 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:116 |
| Stem-50 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:117 |
| Stem-45 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:118 |
| Stem-40 | TTAACTATGCGGCATTTAACTATGCGGCATTTAACTATGC | SEQ ID NO:119 |
| Stem-35 | TTAACTATGCGGCATTTAACTATGCGGCATTTAAC | SEQ ID NO:120 |
| Stem-30 | TTAACTATGCGGCATTTAACTATGCGGCAT | SEQ ID NO:121 |
| Stem-25 | TTAACTATGCGGCATTTAACTATGC | SEQ ID NO:122 |
| Stem-20 | TTAACTATGCGGCATTTAAC | SEQ ID NO:123 |
| Stem-15 | TTAACTATGCGGCAT | SEQ ID NO:124 |
| Stem-10 | TTAACTATGC | SEQ ID NO:125 |
| Stem-5 | TTAAC | SEQ ID NO:126 |

**[00184]** The oligonucleotides were designed to contain a 15-mer probe (CTGGCAGCAGCCACT) (SEQ ID NO:73) at their 5'-end and connected to variable sizes of non-probe sequence from 0 to 85 nucleotides in length. Additionally, a single base mismatch 15-mer (CTGGCAGTAGCCACT) (SEQ ID NO:91) probe and a single base deletion 14-mer (CTGGCAGAGCCACT) (SEQ ID NO:109) probe were also synthesized on the chip as control sequences. Oligonucleotides from 5 to 100 nucleotides in length were synthesized on the chip, and the two control sequences were arranged side by side in the array for comparison purpose. After the oligomers were synthesized on the array chip, the chip was deprotected with EDA at room temperature for 2 hours and fill with 6xSSPE buffer. The 15 nucleotide target

oligonucleotide labeled with a Cy3 dye was hybridized to the chip in 6xSSPE for 2 hours at room temperature, and the chip was subsequently washed with 0.001xSSPE buffer. As illustrated in Figure 25 and shown in Figure 26, the presence of fluorescence on the chip after the hybridization assay demonstrates that 100-mer oligonucleotides were synthesized on the chip. Additionally, the fluorescence intensity profile indicated a stepwise yield of 98.5% for the synthesis of these long oligonucleotides, which is a significant improvement over known methods for synthesizing oligonucleotides on an array chip. In another experiment, a comparison of the per step yield for oligonucleotides 15 to 100 nucleotides in length on a dual chip demonstrated an even higher stepwise yield of 98.9% and 99.1% (figure 27).

**[00187]** The disclosed methods for generating pools of oligomers can also be used to generate an RNAi (RNA interference) chip. 252 oligonucleotides were generated on an RNAi chip using the methods previously outlined, with each oligonucleotide synthesized containing a SAP1 sequence (TGCAGTTAGCTCTTCCASAT) (SEQ ID NO:128) at the 3' end, a variable RNAi specific sequence in the middle (22 nucleotides in length), and a T7 promotor sequence CCTATAGTGAGTCGTATTA) (SEQ ID NO:129) at the 5'-end (total length about 60 nucleotides). In order to cleave the oligonucleotides from the chip, reverse-U was incorporated into the 3'-end of all oligonucleotides. Additionally, the same two control oligonucleotides (puc2PM- (SEQ ID NO:44-perfect match) and Puc2MM- (SEQ ID NO:45-mismatch) as disclosed in example 3 were also synthesized on the RNAi chip. The quality of the oligonucleotides synthesized on the RNAi chip was also analyzed by hybridization with Cy3 labeled 15-mer Puc2 target as outlined in Example 3.

## II. ADDITION OF SEQUENCE LISTING

Please place the attached paper copy of the "Sequence Listing" in the captioned application beginning as a new page after the "Abstract of the Disclosure."

## III. CONCLUSION

Applicants believe that a full and complete reply has been made to the Request to Comply with Sequence Rules and, as such, the present application is in condition for allowance. Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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